

REMARKS

Anticipation Rejection of Claims 1 and 3

On page 2 of the Office Action, claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Bost (US 3,963,571).

Applicants respectfully submit that the present invention is not anticipated by (or obvious over) Bost, and request that the Examiner reconsider and withdraw this rejection in view of the following remarks.

1) Bost discloses a **two-stage** reaction in which $C_{18}\alpha$ -hydroxycycloalkanone is dehydrated to form cyclooctadecenone, which is subsequently reacted with hydrogen to form cyclooctadecanone (reaction formulae (5) and (6) in the second column).

However, the method of the present invention is to conduct catalytically a dehydration reaction and a hydrogenation reaction simultaneously in a **single** pot in the coexistence of an acid catalyst and a hydrogenation catalyst and in the presence of hydrogen.

Accordingly, Applicants submit that the present invention is completely different from the method set forth in Bost, which conducts the two-stage reaction separately and sequentially.

2) The Examiner recognizes that a reaction conducted in the presence of zinc and hydrochloric acid is disclosed in Bost. However, this reaction disclosed by Bost and using zinc and hydrochloric acid is a reaction in which a cyclic α -hydroxyketone (cyclic acyloin) is reduced directly to a cyclic ketone (reaction formula (4) in the

second column), different from the reaction of the present invention, as discussed in detail subsequently in this response.

Further, Bost discloses in the specific description relating to the direct reduction using zinc and hydrochloric acid that, to 6.5 g (0.023 mol) of cyclic α -hydroxyoctadecanene, 10 g of zinc was first added under bubbling of hydrogen chloride, and further 2 g of zinc was added twice during reaction whereby 14 g (0.214 mol) of zinc in total was used for reaction (lines 50 to 65 of the fourth column). Namely, in the above reaction, 9.3 equivalents of zinc were used relative to acyloin as the raw material.

Moreover, in the attached reference material 1 (ORGANIC SYNTHESES VOL IV) that describes the reaction disclosed by Bost, relative to 42.5 g (0.25 mol) of sebacoin as a raw material, 40.5 g (0.62 mol) of zinc dust and 90 ml of concentrated hydrochloric acid were used at first, and that during reaction, an additional 90 ml of concentrated hydrochloric acid was added, so 180 ml (2.16 mol) of concentrated hydrochloric acid were used in total. These quantities calculate to give 2.5 equivalents of zinc and 8.64 equivalents of hydrochloric acid relative to one equivalent of sebacoin as a raw material. In addition, reference material 1 includes the expressions "remaining zinc" or "residual zinc", indicating that zinc is consumed during reaction.

As is evident from the descriptions of Bost and reference material 1 cited heretofore, in the direct reductive reaction using zinc and hydrochloric acid, the two compounds are not to be defined as "catalysts" by any means. In view of this fact,

the method of the present invention *in which a dehydration reaction is conducted catalytically and simultaneously with a hydrogenation reaction* is clearly different from the reaction set forth in Bost.

3) Further, the Examiner apparently considers that the reaction achieving direct reduction with use of zinc and hydrochloric acid and the one sequentially achieving dehydration and hydrogenation fall under a single reaction scheme. However, the reaction schemes for these two reactions are neither common to each other nor to be combined together.

For example, in the attached reference material 2 (COMPREHENSIVE ORGANIC TRANSFORMATIONS, R.C. Larock, Wiley-VCH, 1999), which collects a variety of reactions of conventionally known functional groups, such examples that zinc and/or hydrochloric acid act as catalysts are not set forth in the item for catalytic hydrogenation of alkenes.

Thus, it is evident that the reaction using zinc and hydrochloric acid cannot be applied to the hydrogenation reaction for a double bond, and that those skilled in the art have no motivation for combining these reactions. Moreover, Bost has no teaching or suggestion of the reaction of the present invention.

In particular, it is noted that the Examiner is combining elements of two separate, alternate processes in Bost and asserting that they are all present in a single process.

That is, Bost discloses at column 2, lines 36-42 "cyclic α -hydroxyketones (cyclic acyloin) which can be reduced directly to the cyclic ketones by hydrogen iodide or zinc and hydrochloric

acid. Alternatively, the cyclic acyloins can be dehydrated to the cyclic unsaturated ketones which can be selectively hydrogenated to the cyclic saturated ketone" (emphasis added).

Thus, Bost discloses the use of zinc and hydrochloric acid in one process (a direct reduction process), and the use of dehydration and then hydrogenation is a different, alternate process. Bost does not disclose the use of zinc and hydrochloric acid in a process which uses dehydration and hydrogenation, contrary to the Examiner's assertion.

Indeed, Bost specifically discloses the word "or" at column 2, line 62, after reaction 4 (which is the reaction that uses zinc and hydrochloric acid) and before reaction 5 (the dehydration reaction) and reaction 6 (the hydrogenation reaction).

Further, the example disclosure at column 4, line 50 to column 5, line 3 cited by the Examiner only involves the direct reduction method using zinc and hydrochloric acid; the presence of hydrogen itself is not disclosed.

Accordingly, it is submitted that the Examiner's reliance on the disclosure at column 2, lines 45-68, and at column 4, line 50 to column 5, line 3, for a single reaction scheme in which zinc and hydrochloric acid are used together with dehydration and hydrogenation is improper, and that Bost neither teaches nor suggests the present invention, such that the present invention is not anticipated by (or obvious over) Bost.

As discussed above, the reaction of the present invention is completely different from the one set forth in Bost, and is not obvious over the description of Bost. Accordingly, Applicants submit that the present invention is patentable over Bost, and withdrawal of this rejection is respectfully requested.

Obviousness Rejections of Claims 2 and 4

On page 3 of the Office Action, claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bost (US 3,963,571) and Nakajima et al (US 5,300,654) in combination. Further, on page 4 of the Office Action, claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bost and Nakajima et al as applied to claim 2 above, and further in view of Makita (JP 202220361).

Applicants respectfully submit that claims 2 and 4 are not obvious over the cited art combinations, and request that the Examiner reconsider and withdraw these rejections in view of the following remarks.

1) What is described in Nakajima is a dehydration reaction, and, as the Examiner admits, is different from the direct reductive reaction disclosed by Bost.

In addition, as stated previously, hydrochloric acid cannot be regarded as a reaction catalyst in the direct reductive reaction using zinc and hydrochloric acid.

Accordingly, it is evident that the hydrochloric acid used for the direct reductive reaction set forth in Bost is not equivalent to the dehydration catalyst disclosed by Nakajima.

2) On the other hand, as stated above, not only has no catalytic hydrogenation reaction with use of zinc and/or hydrochloric acid been known, but also zinc and/or hydrochloric acid in the reaction set forth in Bost cannot be regarded as catalysts.

Accordingly, it is evident that the zinc used for the direct reductive reaction set forth in Bost is not equivalent to the catalyst such as palladium, etc. set forth in Makita.

3) As has been discussed hereinabove, it is evident that those skilled in the art have no motivation for combining the catalyst of Nakajima or Makita with the reaction set forth in Bost.

Thus, Applicants submit that the method of the present invention is a new and unobvious one in which a dehydration reaction and a hydrogenation reaction are catalytically conducted in the coexistence of an acid catalyst and a hydrogenation catalyst and in the presence of hydrogen, i.e., in which the two reactions are conducted simultaneously in a single pot, thereby achieving the advantageous effect of efficient production of the ketone in concern with a high yield.

Since Nakajima and Makita do not make up for the deficiencies of Bost, it is submitted that claims 2 and 4, which depend on claim 1, are not obvious for at least the reasons given above with respect to claim 1.

As discussed above, the reaction in the present invention is completely different from that of Bost, and the method of the present invention is not described in Bost, Nakajima and Makita, so Applicants submit that the present invention would not have been reached even if Nakajima and Makita were combined with Bost. Accordingly, withdrawal of these rejections is respectfully requested.

Obviousness Rejection of Claims 5 and 6

On page 4 of the Office Action, claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bost et al and Nakajima et al and further in view of Makita.

In response, Applicants submit that for the same reasons as those set forth above, the present invention would not have been attained even if Bost, Nakajima and Makita were

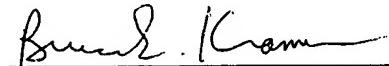
combined together. In this regard, it is submitted that when the teachings of the cited art are fairly considered, Nakajima and Makita do not make up for the deficiencies of Bost as discussed above. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Bruce E. Kramer
Registration No. 33,725

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: October 28, 2005

3. Methods of Preparation

1,2-Cyclodecanediol has been prepared by the hydrogenation of sebacoin in the presence of Raney nickel¹ or platinum,² by the reduction of sebacoin with aluminum isopropoxide³ or lithium aluminum hydride,⁴ and by the oxidation of cyclodecene with osmium tetroxide and pyridine.⁵

¹ Cornell University, Ithaca, New York.

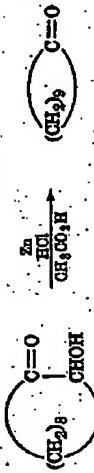
² Org. Syntheses Coll., Vol. 2, 142 (1942).

³ Prelog, Schenker, and Genthard, Helv. Chim. Acta, 38, 1095 (1955).

⁴ Drey, Bothmer, By, and Wurch, Helv. Chim. Acta, 38, 1095 (1955).

⁵ Blomquist, Burgess, and Slesky, J. Am. Chem. Soc., 74, 3636 (1952).

CYCLODECANONE*



Submitted by ARTHUR C. CORP, JOHN W. BAXTER, and RONALD DEAN SMITH¹

Checked by N. J. LEONARD and J. C. LITTLE²

1. Procedure

A 1-l. round-bottomed three-necked flask is fitted with a sealed stirrer (Note 1), a dropping funnel, and a reflux condenser, through which a thermometer extends nearly to the bottom of the flask. In the flask are thoroughly mixed 40.5 g. (0.62 g. atom) of zinc dust (Note 2) and 100 ml. of glacial acetic acid, and to this mixture is added 42.5 g. (0.25 mole) of sebacoin (p. 840) (Note 3). The mixture is stirred rapidly, and 90 ml. of concentrated c.p. hydrochloric acid is added dropwise during a period of 5 to 10 minutes, or as fast as control of foaming and temperature permits. The temperature must be kept between 75 and 80° (Note 4), and cooling by a water bath may be necessary during the addition of the hydrochloric acid. Stirring is continued for 1.5 hours at 75–80°. Thirty minutes after the initial addition of hydrochloric acid, and again 30 minutes later, 90-ml. portions of concentrated hydrochloric acid are added to

the mixture while the temperature is maintained at 75–80°. After the reaction is complete, the remaining zinc is separated from the cooled mixture by decantation (Note 5). The liquid phase is diluted with 700 ml. of saturated aqueous sodium chloride solution, and extracted with four 250-ml. portions of ether, each of which is first used to wash the residual zinc (Note 6). The ether extracts are combined and washed with 250 ml. of saturated sodium chloride solution, three 250-ml. portions of 10% sodium carbonate solution (foaming), and finally 250 ml. of saturated sodium chloride solution. The ethereal solution is dried over anhydrous magnesium sulfate (about 25 g. is needed). After the drying agent has been removed by filtration and the solvent by distillation, the residue is distilled at reduced pressure through an efficient column (Note 7). After a small fore-run consisting mostly of cyclodecane, cyclodecanone is collected at 99–101°/8 mm. The yield is 29–30 g. (75–78%), ρ_D^{25} 1.4808–1.4810 (Note 8).

2. Notes

1. A metal stirrer must not be used. A simple glass stirrer with a ball-joint seal is satisfactory.
2. Mallinckrodt technical grade may be used. If Mallinckrodt analytical reagent zinc dust is used, the reaction temperature must be maintained at 50–55° instead of 75–80°.
3. Pure sebacoin gives a colorless product. A sebacoin-sebacil mixture must first be purified by recrystallization from pentane as described (p. 841). The sebacil apparently is not reduced completely according to the accompanying directions and thus may contaminate the product (see Note 7).
4. The reaction temperature is important. At temperatures below 75° some sebacoin remains unreduced, while at temperatures above 80° considerable cyclodecane is formed. The submitters report that the reaction run at the reflux temperature gives cyclodecanone in 27% yield and cyclodecane in 32% yield.
5. The product should be isolated and distilled as quickly as possible inasmuch as the unreacted sebacoin is readily oxidized to sebacil, which cannot be separated from the cyclodecanone by simple distillation.
6. The residual zinc may be pyrophoric.

7. For efficient separation of cyclodecane from cyclohexane,
a. 60-cm. column of the simple Podbieliak type⁸ may be used.
Removal of sebacil cannot be accomplished readily by fractional
distillation, since cyclohexanone and sebacil have virtually identical
boiling points.

8. Cyclohexanone regenerated from its semicarbazone, m.p.
203.5°–205.5°, has n_D^{25} 1.4816.

3. Methods of Preparation

The procedure described is a modification of the directions of Prelog, Frankiel, Kobelt, and Barman.⁴ Cyclohexanone has been prepared by the dehydration of sebacin followed by catalytic hydrogenation,⁵ by the pyrolysis of the thorium or yttrium salt of nonane-1,9-dicarboxylic acid,⁶ and by the ring enlargement of cyclononanone,⁷ as well as by the reduction of sebacin.⁸

¹ Massachusetts Institute of Technology, Cambridge, 39, Massachusetts.

² Brown and Berkowski, *J. Am. Chem. Soc.*, 74, 1901 (1952).

³ Cason and Rapoport, *Laboratory Test in Organic Chemistry*, 2nd. ed., p. 294, Prentice-Hall, Englewood Cliffs, New Jersey, 1952.

⁴ Prelog, Frankiel, Kobelt, and Barman, *Ref. Chem. Acta*, 30, 1741 (1947).

⁵ Stoll, *Ref. Chem. Acta*, 30, 1837 (1947).

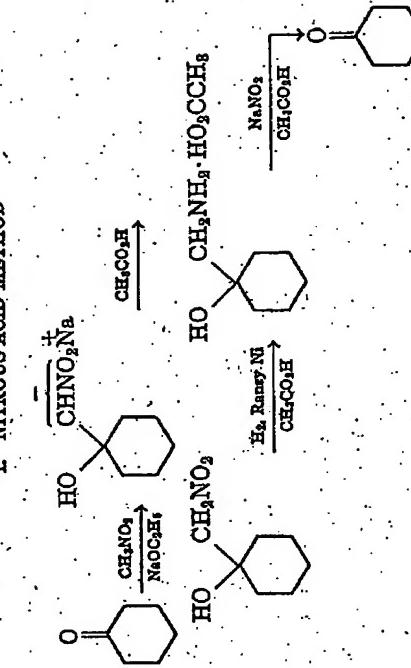
⁶ Ruzicka, Stoll, and Schmid, *Helv. Chim. Acta*, 9, 249 (1926); 11, 670 (1928).

⁷ Kohler, Fisher, Potter, and Thompson, *J. Am. Chem. Soc.*, 61, 1037 (1939).

⁸ Blomquist, Burge, and Sutty, *J. Am. Chem. Soc.*, 74, 3636 (1952).

CYCLOHEPTANONE*

I. NITROUS ACID METHOD



Submitted by HERBERT J. DARNEN, JR., HOWARD J. KINGDON, ROBERT H. WARD,
DAVID L. PEARSON, and ARTHUR G. ANDERSON, JR.
Checked by ALBERT C. COPE, WARREN N. BAXTER, and RONALD J. CUTTER.

1. Procedure

[Caution] The sodium salt of 1-(nitromethyl)cyclohexanol may be an explosive (Note 1).

A solution of sodium ethoxide is prepared by adding 57.5 g. (2.5 g. atoms) of clean sodium to 1.2 l. of absolute ethanol (Note 2) in a 3-l. three-necked flask equipped with an Allihn reflux condenser fitted with a drying tube, a large sturdy sealed Hershberg stirrer, and a dropping funnel. After the sodium has dissolved, the solution is cooled to 40° and the condenser is replaced by a thermometer extending into the liquid. A mixture of 245.5 g. (258.5 ml., 2.5 moles) of redistilled cyclohexanone and 198 g. (175 ml., 3.25 moles) of redistilled nitromethane (Note 3) is added dropwise with vigorous stirring over the course of about 3 hours at a rate that maintains an internal temperature of 45 ± 3° (Note 4). After addition is complete, the white, pasty mass is stirred for an additional 3 hours without cooling or heating and

COMPREHENSIVE ORGANIC TRANSFORMATIONS

**A Guide to
Functional Group Preparations
Second Edition**

**By
Richard C. Larock**



WILEY-VCH

New York • Chichester • Weinheim • Brisbane • Singapore • Toronto

The book is printed on acid-free paper.®

Published by John Wiley & Sons, Inc.

Copyright © 1999 by Richard C. Larock. All rights reserved.

Published simultaneously in Canada.

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except as permitted under Sections 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher, or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400, fax (978) 750-4744. Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 605 Third Avenue, New York, NY 10158-0012, (212) 850-6011, fax (212) 850-6008, E-Mail: PERMREQ @ WILEY.COM.

For ordering and customer service, call 1-800-CALL-WILEY.

Library of Congress Cataloging in Publication Data

Larock, Richard C.

Comprehensive organic transformations : a guide to functional group preparations / by Richard C. Larock – 2nd ed.

p. cm.

Includes index.

ISBN 0-471-19031-4 (cloth : alk. paper)

1. Organic compounds—Synthesis. I. Title.

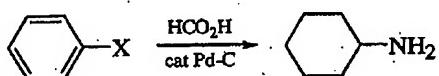
QD262.L355 1999

98-37314

547'.2—dc21

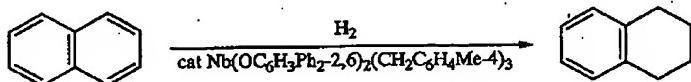
Printed in the United States of America

10 9 8 7 6 5 4



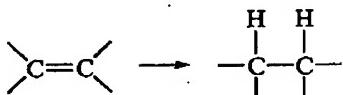
$X = \text{NO, N}_3, \text{NO}_2, \text{NH}_2, \text{NR}_2$

TL 33 7477 (1992)



JACS 114 1927 (1992)

3. Alkenes



3.1. Catalytic Hydrogenation

Reviews:

- R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York (1965)
- P. N. Rylander, "Catalytic Hydrogenation over Platinum Metals," Academic Press, New York (1967)
- M. Freifelder, "Practical Catalytic Hydrogenation," Wiley-Interscience, New York (1971), Chpt 9
- B. R. James, "Homogeneous Hydrogenation," J. Wiley, New York (1973)
- F. J. McQuillin, "Homogeneous Hydrogenation in Organic Chemistry," D. Reidel, Boston (1976)
- A. P. G. Kieboom and F. van Rantwijk, "Hydrogenation and Hydrogenolysis in Synthetic Organic Chemistry," Delft University Press, Delft (1977)
- M. Freifelder, "Catalytic Hydrogenation in Organic Synthesis: Procedures and Commentary," J. Wiley & Sons, New York (1978), Chpt 4
- Syn 85 (1981) (homogeneous asymmetric hydrogenation)
- Chem Rev 85 129 (1985) (heterogeneous catalytic transfer hydrogenation)
- "Asymmetric Synthesis," Ed. J. D. Morrison, Academic Press, New York (1985), Vol 5, Chpts 2, 3, 10
- P. N. Rylander, "Hydrogenation Methods," Academic Press, New York (1985), Chpt 2
- "Comprehensive Organic Synthesis," Eds. B. M. Trost and I. Fleming, Pergamon, Oxford (1991), Vol 8, Parts 3.1 and 3.2, pp 417-470

3.1.1. Selective hydrogenation catalysts

5% Ru on Norit

JOC 24 708 (1959)

RuCl₂(PPh₃)₃

CL 1083 (1977) (polyenes to monoenes)

NaBH₄, CoCl₂ (mono > di > tri > tetrasubstituted)

JOC 44 1014 (1979)

JACS 108 67 (1986)

Rh-C

TL 32 2735 (1991) (fluoroalkenes); 36 7949 (1995) (enamide)

Rh-Al₂O₃

Org Syn Coll Vol 6 371 (1988)

TL 29 3171 (1988)

ClRh(PPh ₃) ₃ (Wilkinson's catalyst)	Discuss Faraday Soc 46 60 (1968) Chem Rev 21 73 (1973) Syn 329 (1978) Prog Inorg Chem 28 63 (1981)
ClRh[P(<i>p</i> -Tol) ₃] ₃ (regioselective)	TL 33 5547 (1992)
[Rh(NBD)(dppb)]BF ₄	CC 348 (1982) (syn to allylic, homoallylic OH) JACS 106 3866 (1984) (syn to OH); 107 4339 (1985) (syn to OH); 108 2476 (1986); 112 5290 (1990) (homoallylic OH) TL 25 4637 (1984) (allylic OH); 26 6005 (1985) (homoallylic OH); 28 3659 (1987)
[Rh(COD)(dppb)]BF ₄	JACS 115 7152 (1993) TL 34 4939 (1993)
[Rh(NBD)(dppb)]OTf	Org Syn Coll Vol 8 420 (1993)
[Ir(COD)(dppb)]BF ₄	TL 25 4637 (1984) (allylic OH)
[Ir(COD)(py)(PCy ₃)]PF ₆	TL 22 303 (1981) (α face of steroids); 25 4637 (1984) (allylic, homoallylic OH); 26 6005 (1985) (homoallylic OH) JACS 105 1072 (1983) (syn to OH); 106 3866 (1984) (syn to OH); 109 6493 (1987) (syn to CONR ₂); 113 4926, 4931 (1991) (syn to CONR ₂) Organomet 2 681 (1983) (syn to OH) JOC 50 5905 (1985) (syn to CO ₂ R, CONR ₂); 51 2655 (1986) (syn to OH, CO ₂ R, C=O, OMe); 60 5102 (1995) (syn to OH) JOC 38 2226 (1973); 46 1263 (1981) JOC 52 5695 (1987) (least substituted double bond)
Nickel boride (P-2)	JOC 45 1937, 1946 (1980)
LaNi ₅ H ₆	TL 32 2735 (1991) (fluoroalkenes) TL 32 2735 (1991) (fluoroalkenes)
NaH, NaO- <i>t</i> -Am, Ni(OAc) ₂	TL 33 121 (1992)
Pd-C	TL 34 3075 (1993)
Pd-BaSO ₄	JACS 94 8716 (1972) (polyene to monoene)
Montmorillonite-PPh ₂ -PdCl ₂	Adv Catalysis 9 727 (1957)
Pd(hfacac) ₂ , Me ₃ Si(OSiHMe) _n OSiMe ₃	
PtCl ₂ , (Et ₄ N)SnCl ₃ or (Ph ₃ PMc)SnBr ₃	
PtO ₂	

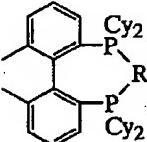
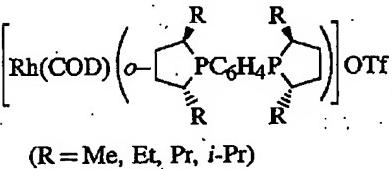
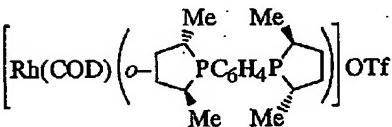
3.1.2. Enantioselective hydrogenation catalysts

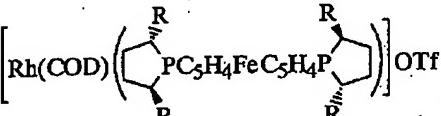
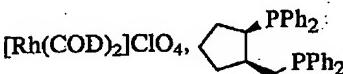
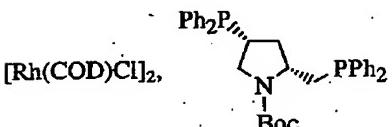
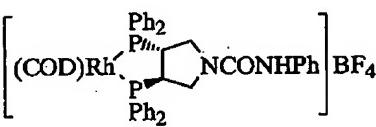
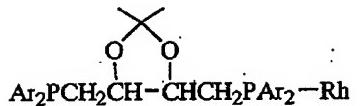
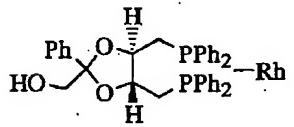
Reviews:

- H. B. Kagan, "Comprehensive Organometallic Chemistry," Eds. G. Wilkinson and F. G. A. Stone, Pergamon, Oxford (1982), Vol 8, p 463
 Pure Appl Chem 56 99 (1984)
 "Asymmetric Catalysis," Ed. B. Bosnich, NATO ASI Ser. E, No. 103, Martinus Nijhoff, Dordrecht (1986), Chpt 2
 Chem Rev 92 1051 (1992) (asymmetric)

SL 169 (1992) (Rh bis-phosphines)
 "Catalytic Asymmetric Synthesis," Ed. I. Ojima, VCH, New York (1993), Chpt 1
 Houben-Weyl, "Methods of Organic Chemistry," 4th ed, Vol E21d, G. Thieme, Stuttgart-New York
 (1995), p 4239

<u>Catalyst</u>	<u>Substrate</u>	
Ti(BINOL),  n-BuLi, PhSiH ₃	trisubstituted aryl alkenes	JACS 115 12569 (1993)
Ru(DIPAMP)(2-Me-allyl) ₂ or Ru ₂ X ₂ (DIPAMP)	α,β-unsaturated carboxylic acids, α-amido acrylic acid	TL 33 5343 (1992)
Ru(2-Me-allyl)(diphosphine)	α,β-unsaturated carboxylic acid	Tetr Asym 2 43 (1991)
Ru ₂ Cl ₄ (BINAP)	α-amido-α,β-unsaturated lactam enones	TL 35 3239 (1994) JOC 60 357 (1995)
Ru ₂ Cl ₄ (BINAP) ₂ (NEt ₃)	α-amidoacrylic acids unsaturated dicarboxylic acids α,β-unsaturated lactone and anhydride α-alkylidene lactams 2-fluoro-2-alkenoic acids enones vinylic ester vinylic ether	CC 922 (1985) TL 28 1905 (1987); 35 835 (1994) TL 33 635 (1992) TL 36 7379 (1995) TL 33 7877 (1992) JOC 60 357 (1995) JOC 60 357 (1995) JOC 60 357 (1995)
[(arene)RuX(BINAP)]X	allylic alcohol, α,β-unsaturated carboxylic acid α,β-unsaturated lactone, enone	CC 1208 (1989) JOC 59 3064 (1994) TL 33 635 (1992) JOC 60 357 (1995)
Ru(BINAP)(Ph)Cl	enamide	JOC 60 4324 (1995)
RuHCl(BINAP) ₂	α-amidoacrylic acids unsaturated dicarboxylic acids	CC 922 (1985) TL 28 1905 (1987)
Ru(OAc) ₂ (BINAP)	enamides allylic alcohols homoallylic alcohols enone	JACS 108 7117 (1986) JOC 59 297 (1994) JACS 109 1596 (1987) JOC 53 708 (1988) TL 34 7359 (1993) JACS 109 1596 (1987) TL 33 635 (1992) JOC 60 357 (1995)
	α-amido acrylate esters vinylic ether vinylic ester α,β-unsaturated carboxylic acid	JOC 59 3676 (1994) JOC 60 357 (1995) JOC 60 357 (1995) JOC 52 3174 (1987) TL 31 7189 (1990) SL 501 (1994)

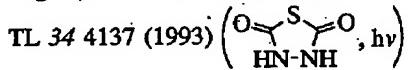
<u>Catalyst</u>	<u>Substrate</u>	
Ru(OAc) ₂ (BINAP) (<i>continued</i>)	β,γ -unsaturated carboxylic acids	JOC 52 3174 (1987) TL 31 7189 (1990)
Ru(OAc) ₂ (tolbinap)	allylic alcohols	TL 31 549 (1990)
Ru(OAc) ₂ (H ₈ -BINAP)	α,β -unsaturated carboxylic acid	SL 501 (1994)
Ru(O ₂ CCF ₃) ₂ (BINAP)	allylic alcohols	TL 29 5343 (1988)
[Rh(NBD)Cl] ₂ , Ph ₂ PCH ₂ CH(CH ₃)PPh ₂	α -amidoacrylic acids and esters	JOC 56 1783 (1991)
[Rh(NBD) ₂]ClO ₄ , Ph ₂ PCH ₂ CH(CH ₃)PPh ₂	α -amidoacrylic acids and esters	JACS 110 5491 (1978)
[Rh(COD)Cl] ₂ , norphos	α -amidoacrylic acid	Angew Int 18 620 (1979)
[Rh(NBD)Cl] ₂ , norphos	α -amidoacrylic acid and ester	JOC 56 1783 (1991)
[Rh(NBD)Cl] ₂ , S,S-chiraphos	α -amidoacrylic acid	JOC 56 1783 (1991)
[Rh(NBD)(S,S-chiraphos)]ClO ₄	α -amidoacrylic acids and esters	JACS 99 6262 (1977); 115 4040 (1993) JOC 52 5143 (1987)
[Rh(NBD)(BINAP)]ClO ₄	α -amidoacrylic acids α -amidoacrylic acids and esters	JACS 102 7932 (1980) Tetr 40 1245 (1984)
[Rh(NBD)(BINAP)]BF ₄	α,β -unsaturated ester	JACS 108 2476 (1986)
	Rh(NBD)X (X = Cl, ClO ₄)	α -amidoacrylate ester, itaconic acid and ester
[Rh(NBD)(Josiphos)]BF ₄	α,β -unsaturated ester, α -amidoacrylate ester	JACS 116 4062 (1994)
[Rh(NBD)(diPAMP)]BF ₄	α -amidoacrylamide	TL 35 5785 (1994)
[Rh(NBD)(Ph-CAPP)]BF ₄	α -amidoacrylamide	TL 35 5785 (1994)
	α -amidoacrylate esters, enol acetates	JACS 113 8518 (1991); 115 10125 (1993); 116 10847 (1994); 117 9375 (1995)
	α -amidoacrylate ester	JACS 117 9375 (1995)

	α -amidoacrylate ester, α,β -unsaturated ester	TL 35 9363 (1994)
(R = Me, Et)		
[Rh(COD)(anthraphos)]BF ₄	α -amidoacrylic acid	TL 35 7593 (1994)
[Rh(COD)(o-EtC ₆ H ₄ PPhCH ₂ CH ₂ PPh-C ₆ H ₄ Et-o)]BF ₄	α -amidoacrylic acids and esters	TL 36 8271 (1995)
[Rh(COD) ₂]BF ₄ , R ₂ PCHMeFer-FerCH-MePR ₂	α -amidoacrylate esters	JACS 117 9602 (1995)
	α -amidoacrylic acid	SL 49 (1991)
	acrylic acid	SL 155 (1993)
	acrylic acid	SL 155 (1993)
[RhL(COD)]SbF ₆ (L = glucose 3,4-diphosphinates)	α -amidoacrylic acids and esters	JACS 116 4101 (1994)
Rh(O ₂ CCF ₃) ₂ (tolbinap)	enamides	TL 28 4829 (1987)
chiral (aminoalkyl)ferrocenylphosphine-Rh	trisubstituted acrylic acids	JACS 109 7876 (1987)
chiral pyrrolidinodiphosphines-Rh	itaconic acid; α,β -unsaturated acids, esters, and ketones; α -amidoacrylic acids	TL 29 5969 (1988) CL 567 (1978) Ber 119 3326 (1986) Angew Int 27 1180 (1988) Syn 743 (1989) JOMC 387 209 (1990) TL 32 3671 (1991) JACS 115 152 (1993)
diop-Rh	α,β -unsaturated carboxylic acids, α -amidoacrylic acids and esters	CC 481 (1971) JACS 94 6429 (1972) JOC 56 1783 (1991)
	α,β -unsaturated ester	TL 29 4755 (1988); 30 735 (1989); 31 261 (1990) JOC 60 4339 (1995)
	α -amidoacrylic acid and ester	TL 35 6071 (1994)

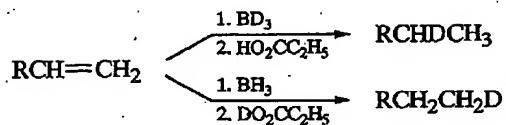
Catalyst	Substrate	
Ph ₂ PCH(CH ₂ OR)CH ₂ PPh ₂ -Rh	α -amidoacrylic acids and esters	J Chem Res (S) 117 (1982)
α -Ph(Me)PC ₆ H ₄ P(Me)Ph-Rh(I)	α -amidoacrylate ester	JACS 115 4040 (1993)
(R,R-1,2-bis((phenyl- α -anisoyl)-phosphino)-ethane)-Rh(I)	various α -amidoacrylate derivatives	JACS 99 5946 (1977); 109 1746 (1987); 115 4040 (1993)
organosamarium compound	alkenes	JACS 114 2761 (1992)

3.2. Dilimide Reduction (HN=NH)

J Chem Ed 42 254 (1965) (review)
 Angew Int 4 271 (1965) (review)
 Syn Commun 12 287 (1982) (HONH₂, EtOAc)
 JOC 52 4665 (1987); 57 6092 (1992) (both TsNHNH₂, NaOAc); 59 4346 (1994) (N₂H₄, NaIO₄)
 JACS 110 1529 (1988) (N₂H₄, air, CuSO₄)
 Org Rxs 40 91 (1991) (review)



3.3. Hydroboration-Protonolysis



JACS 81 4108 (1959)
 JOMC 255 135 (1983)

3.4. Metal Hydrides

LiH, VCl ₃ (RCH=CH ₂ only)	JOC 45 1041 (1980)
NaH, NaO-t-Bu, FeCl ₃	TL 3947 (1977)
NaH, NaO-t-Am, Ni(OAc) ₂	TL 1069 (1977)
NaBH ₄ , CoCl ₂	JACS 108 67 (1986)
NaBH ₄ , cat NiCl ₂ ·6H ₂ O	JACS 104 5781 (1982) JOC 56 1192 (1991)
NaBH ₃ CN, HCl	JACS 113 5775 (1991)
LiAlH ₄	TL 31 553 (1990)
LiAlH ₄ , TiCl ₄ or ZrCl ₄	TL 15 (1976) JOMC 142 71 (1977)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.